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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,838	11/29/2004	Shmuel A. Ben-Sasson	24348-501 NATL	6386

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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 10/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,838	BEN-SASSON ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15-20,26,27,31-50,53-56,63 and 68-83* is/are pending in the application.

4a) Of the above claim(s) *19,20,39-50,54-56,63,76,79,80,82 and 83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 15-18, 26, 27, 31-38, 53, 68-75, 77, 78 and 81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants argue that claim 63 is directed to the invention elected in the response filed November 18, 2005, in which SEQ ID NO: 24 (a peptide derived from a human neurokinin receptor) was provisionally elected. Hence, applicants requests that the claim 63 be considered pending and examined.

Applicant's arguments filed 9/7/06 have been fully considered but they are not persuasive. Because, applicants originally elected group 16 directed to SEQ ID NO: 16 in their reply to election restriction on 11/18/2005. Claim 63 belong to group 150 and therefore it is properly withdrawn as being drawn to non-elected invention in our office action dated 5/26/06.

Applicant's amendments to claims and remarks filed on 9/7/06 are here by acknowledged.

Claims 1 and 81 have been amended.

Claims 1, 15-20, 26, 27, 31-50, 53-56, 63 and 68-83 are pending.

Claims 2-14, 21-25, 28-30, 51, 52, 57-62 and 64-67 have been canceled.

Claims 19, 20, 39-50, 54-56, 63, 76, 79 and 80 are withdrawn from further consideration as being drawn to non-elected invention.

Claims 82 and 83 are withdrawn from further consideration as being drawn to non-elected species.

Claims 1, 15-18, 26, 27, 31-38, 53, 68-75, 77, 78 and 81 are examined on the merit.

Any objections and rejections not specifically mentioned in this office action is to be

considered withdrawn.

Response to Arguments/Remarks

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 15-18, 26, 31, 32, 53 and 81 remain rejected under 35 U.S.C. 102(b) as being anticipated by EP 1 136 557 A1 of Schilfgaarde, et al as stated in our previous office action dated 5/26/06.

Applicants argue that the SEQ ID No: 4 of the cited reference wherein the argument of Examiner that first 2 amino acid residues or 26-205 residues could not serve as an effector molecule. Applicants argue that the terms 'fusion', 'fused' or 'attached' refers to specific interactions that result in two or more separate molecules showing a preference for one another relative to a third molecule (page 10, paragraph 2). Applicants further argue that, "In contrast, amino acid residues 1-25 or 3-205 of Schilfgaarde's SEQ ID NO: 4 (a portion of which forms the penetrating peptide sequence SEQ ID NO: 1 recited by the claimed invention) cannot be interpreted as a penetrating module comprising a conjugate between an effector and a penetrating peptide, which show a preference for one another relative to some other molecule in accordance with the claimed invention. Rather, amino acid residues 1-25 or 3-205 of Schilfgaarde's SEQ ID

NO:4 is simply contiguous amino acid residues from the same origin. While the effector portion of the penetrating module of the claimed invention can include, *inter alia*, DNA, RNA, or proteins (see specification at page 18, lines 1-9), Applicants contend that the specification makes clear that such DNA, RNA, or proteins are not derived from the same origin as is the penetrating peptide" (page 10, paragraph 3).

Applicant's arguments filed 9/7/06 have been fully considered but they are not persuasive. Because, the argument that the first 2 amino acid residues or 26-205 residues of SEQ ID NO: 4 of the cited reference could not serve as an effector molecule is moot. Applicants in their remark **admit** that the effector can be paired with the penetrating peptide via a **peptide linker** which is through an 'amide bond' (page 10, paragraph 2, lines 10 and 11 within the paragraph). Additionally, the effector molecule is a **bioactive peptide** according to claim 15 of the instant application. With regards to argument that the specification makes clear that the penetrating module is a conjugate between at least two compounds between an effector and a penetrating peptide, which show a preference for one another relative to **some other molecule** in accordance with the claimed invention. Applicants further state that SEQ ID NO: 4 of the cited reference is a contiguous amino acid residues from the same origin. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., 'the penetrating module is a conjugate between two molecules from different origins' are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, the cited reference Schilfgaarde discloses that disruption of the HI0638 (SEQ ID NO: 4) by

kanamycin box insertion in H. influenza strain A960053 resulted in loss of penetration into the epithelial cell layers (page 4, [0033]). This means that any disruption in the protein sequence of SEQ ID NO: 4 affects the paracytosis function and hence the sequence beyond the amino acid residues 3-25 has biological function associated with it and hence act as an effector molecule. As indicated in our previous office action dated 5/26/06 (page 4, lines 14-16), the Schilfgaarde reference teaches using recombinant techniques to obtain paracytin peptides fused to other therapeutically active peptides and proteins. Therefore, due to the aforementioned arguments the rejection under 35 USC 102 is proper and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 15-18, 26, 27, 31-38, 53, 68-75 77, 78 and 81 remain rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1 136 557 A1 of Schilfgaarde, et al., in view of Juliano, et al., Current Opinion in Molecular Therapeutics, 2000, 2, 297-303, in view of Lindgren, et al., TIPS, 2000, 21, 99-103, further in view of US 5,286,637 issues to Veronese as stated in our previous office action dated 5/26/06.

Applicants argue that Schilfgaarde does not teach or suggest that a peptide consisting of 3-25 of its SEQ ID NO: 4 (corresponding to SEQ ID NO: 1 of instant application) is useful for translocating a biologically active effector molecule coupled thereto across a biological barrier. Applicants further alleges that Schilfgaarde does not suggest that its full length amino acid sequence be modified in a manner required to meet the invention as recited by independent claims 1 and 81 of the instant application. The argument further includes that on the contrary, "Applicants assert that one of skill in the art reading Schilfgaarde at the time of invention would be led to understand that the full- length sequence of Schilfgaarde's SEQ ID NO: 4 is required for penetration through epithelial cell layers. Accordingly, Schilfgaarde actually teaches away from the claimed invention, which recites, in relevant part, a penetrating peptide consisting of SEQ ID NO: 1 (corresponding to the amino acid residues 3-25 of Schilfgaarde's SEQ ID NO: 4). Furthermore, Schilfgaarde does not teach or suggest any of the other penetrating peptides of SEQ ID NOS: 2-15 and 24-29".

With regards to combination of references, applicants assert that the Examiner improperly relies on hindsight reconstruction. Applicants argue that the mere fact that references can be combined or modified to fit the claimed invention does not render the resultant combination obvious unless the prior art references themselves suggest the desirability of the

combination.

Applicant's arguments filed 9/7/06 have been fully considered but they are not persuasive. Because, the argument that Schilfgaarde does not teach or suggest that a peptide consisting of 3-25 of its SEQ ID NO: 4 (corresponding to SEQ ID NO: 1 of instant application) is useful for translocating a biologically active effector molecule coupled thereto across a biological barrier is not persuasive. It should be noted that the applicants are claiming a penetrating module **comprising** of an effector molecule 'fused', 'coupled' or 'conjugated' to the penetrating peptide and the effector molecule being a 'bioactive peptide' according to claim 15 of the instant application. The fact that the SEQ ID NO: 4 of the cited reference comprising of the instantly claimed peptide SEQ ID NO: 1, wherein the rest of the molecule of the SEQ ID NO: 4 of the cited reference is very much essential for the function of paracytosis as described above in 35 USC 102 section, meets the limitation of the claims 1 and 81.

With regards to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the

teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, suggestions to combine the references stems from the fact that the primary reference teaches using recombinant techniques to obtain paracytin peptides fused to other therapeutically active peptides and proteins. Therefore, paracytin peptides when conjugated to other active peptides or protein would meet the limitations of the instantly claimed invention wherein a penetrating peptide is conjugated to an effector molecule. As stated in our office action dated 2/7/06, Lindgren, et al., teaches conjugation of biomolecules such as peptides, proteins, nucleic acids, etc., to cell penetrating peptides with a further suggestion that drugs and other research tools (diagnostic agents) can be synthesized for cellular delivery. Therefore, the obviousness rejection as stated in our previous office actions 2/7/06 and 5/26/06 is deemed fit and hence maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 31, 33, 34 and 53 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting. Applicants have indicated to file a terminal disclosure in compliance with 37 CFR 1.321(c) upon notification of all allowable subject matter. The rejection is maintained till such time such a terminal disclosure is filed by the applicants and accepted by the Office.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

10/26/06
ANISH GUPTA
PRIMARY EXAMINER

Satyanarayana R. Gudibande, Ph.D.